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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
08/855,402	05/13/97	BRADFIELD	C

EXAMINER	
LU M. T	
ART UNIT	**PAPER NUMBER**
1812	5

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DATE MAILED: 11/24/97

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 1, 2, 4-6, 8-20 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) 1, 2, 4-6, 8-20 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☑ Notice of Reference Cited, PTO-892

☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). 3

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

– SEE OFFICE ACTION ON THE FOLLOWING PAGES –

★ U.S. GPO: 1996-409-290/40029

1) Claims 1, 2, 4 to 6 and 8 to 20 are pending in the instant application. Claims 3 and 7 have been canceled as requested by applicant in Paper Number 2, filed 13 May 1997.

2) The oath or declaration is defective. A new oath or declaration in compliance with 37 C.F.R. § 1.67(a) identifying this application by its Serial Number and filing date is required. See M.P.E.P. §§ 602.01 and 602.02.

The oath or declaration is defective because:

It does not state that the person making the oath or declaration in a continuation-in-part application filed under the conditions specified in 35 U.S.C. § 120 which discloses and claims subject matter in addition to that disclosed in the prior copending application, acknowledges the duty to disclose material information as defined in 37 C.F.R. § 1.56(a) which occurred between the filing date of the prior application and the national or PCT international filing date of the continuation-in-part application.

3) Claims 1, 2, 4 to 6 and 8 to 20 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 to 17 of U.S. Patent No.5,650,283 . Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the patented claims is encompassed in its entirety by the pending claims, which are generic thereto.

The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel,* 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornum,* 686

F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78(d).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4) Claims 1, 2, 4 to 6, 8 to 12 and 14 to 20 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to an Ah receptor protein having that amino acid sequence presented in either SEQ ID NO;2 or 4 of the instant specification because these are the only Ah receptors described therein. These claims currently encompass cells

which are transfected with Ah receptor genes that have yet to be cloned. Amgen Inc. v. Chugai Pharmaceuticals Co. Ltd., 18 U.S.P.Q. 2d, 1016, held that;

> "A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and describe how to obtain it. *See Oka,* 849 F.2d at 583, 7 USPQ2d at 1171. Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property. We hold that when an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, *i.e.*, until after the gene has been isolated"

The text on page 3 of the instant specification discloses that "the AH-receptor exhibits significant polymorphism, both between species and within different strains of the same species". This constitutes an admission by Applicant that the structure and function of one species of AH receptor is not predictive of the structure and function any and all other AH receptors whether they are from the same or different species of organism. Additionally, these claims encompass a cell containing a plasmid which encodes an Ah receptor having other than a natural amino acid sequence. However, the instant specification does not identify those amino acid residues in the amino acid sequences of SEQ ID NOs: 2 and 4 which are essential for the biological activity and structural integrity of those proteins and those residues which are either expendable or substitutable. In the absence of this information a practitioner would have to resort to a

substantial amount of undue experimentation in the form of insertional, deletional and substitutional mutation analysis of over 800 amino acid residues before they could even begin to rationally design a functional Ah receptor protein having other than one of the disclosed natural amino acid sequences. The disclosure of two DNAs encoding Ah receptors with natural amino acid sequences is clearly insufficient support under the first paragraph of 35 U.S.C. § 112 for claims which encompass any and all proteins which might be encompassed by the term "Ah receptor protein". These claims could be construed as "single means" claims since they encompass an assay which employs a nucleic acid encoding any "Ah receptor protein" whereas the instant specification only discloses those two which are known to Applicant.

The current claim limitations are broader in scope to those of claim 7 of U.S. Patent Number 4,703,008 which were held to be invalid under 35 U.S.C. § 112, first paragraph, for want of enablement in Amgen Inc. v. Chugai Pharmaceuticals Co. Ltd., 18 U.S.P.Q. 2d, 1016 (see page 1026, section D). In that instance, a claim to a nucleic acid encoding a polypeptide having an amino acid sequence sufficiently duplicative of the amino acid sequence of erythropoietin (EPO) so as to have a specified biological activity was held to be invalid under 35 U.S.C. § 112, first paragraph, for want of enablement. This limitation is narrower than the "Ah receptor protein" limitation of the instant claims because it contained some material limitation whereas the instant claims do not. The disclosure upon which that claim was based described a recombinant DNA encoding EPO and a few analogs thereof. That disclosure differs from the instant specification because, whereas the instant specification describes two DNAs, each of which encodes a

particular Ah receptor protein, it does not describe even a single variant thereof. The court held that what is necessary to support claims of this breadth is a disclosure sufficient to enable one skilled in the art to carry out the invention commensurate with the scope of the claims. For DNA sequences, that means disclosing how to make and use enough sequences to justify the grant of the claims sought. As indicated, the instant specification is even more limited than the '008 patent because it describes only a single protein and no analogs or mutants thereof and, therefore, provides even less support than the '008 specification for claims of comparable scope and which were held to be invalid in that patent. Applicant should probably review the recent decision in *The Regents of the University of California v. Eli Lilly and Company*, 43 USPQ2d 1398 (CAFC 1997) before responding to this rejection. See M.P.E.P. §§ 706.03(n) and 706.03(z).

5) Claims 1, 2, 4 to 6 and 8 to 20 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5.1) Claims 1, 5, 11 and 15 are incorrect because there is no antecedent basis for "the" Ah receptor, "the" Ah receptor nuclear translocator and "the" dioxin responsive element as these terms are employed in the claims. For example, SEQ ID NOs: 2 and 4 of the instant specification show that there are at least two different proteins which can function as "an" Ah receptor. Claims 2, 4, 6, 8 to 10, 12 and 14 to 20 are incorrect in so far as they depend from any of claims 1, 5, 11 or 15 for this element.

5.2) Claims 1, 5 and 11 are confusing because of the plurality of the term "yeast cells" and "mammalian cells". The plurality of the word "plasmids" is acceptable because the Ah receptor, nuclear translocator and reporter gene of the instant invention can be encoded by separate plasmids which are all contained within a single cell. The instant claims, however, are not limited to a single cell containing all of these elements. As currently written, these claims encompass a mixture of cells, some of which contain a plasmid encoding an Ah receptor and other cells which contain a plasmid encoding a nuclear translocator and/or a reporter gene. These claims are potentially confusing because they are not limited to a plurality of cells in which each cell contains all of the elements which define the instant invention. This ambiguity can be resolved, for example, by addressing claims 1 and 5 to "a genetically engineered viable yeast cell transformed with...".

5.3) Claim 13 is incomplete and, therefore, uninterpretable. Specifically, an ATCC deposit number has been employed as a limiting element but the actual deposit number is not present in this claim.

5.4) Claims 5 and 11 are incorrect because "its binding in dimerization domains" should be "its binding and dimerization domains". These claims are vague and indefinite because it is unclear which binding domain is encompassed by the preceding term since the Ah receptor has both a DNA binding domain and a ligand binding domain.

5.5) Claim 8 is incorrect because there is no antecedent basis for the plural form of "the Ah receptors" in claim 5, from which this claim depends.

5.6) Claim 14 is incorrect because there is no antecedent basis for the "yeast cells of claim 11" in claim 11.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

6) Claims 1, 2, 4, 15, 16 and 18 to 20 are rejected under 35 U.S.C. § 103 as being unpatentable over the Ema et al. publication (BIOCHEM. BIOPHYS. RES. COMM. 184(1):246-253, 15 Apr. 1992) in view of the combination of the Mak et al. (J. Biol. Chem. 264(36):21613-21618, 25 Dec. 1989) and Hoffman et al. (SCIENCE 252:954-958, 17 May 1991) publications. Figure 1 of the Ema et al. publication described a recombinant DNA encoding a murine Ah receptor. The text in the first paragraph of this publication shows that the involvement of Ah

receptors in mediating the effects of environmental pollutants such as dioxin upon animals had been well established in the art at the time of its publication. The text on page 250 of the Ema et al. publication disclosed that the Ah receptor bound ligand in the cytoplasm and, through an interaction with a protein identified therein as "Arnt", was transported to the nucleus where it enhanced the transcription of certain genes by binding to an XRE (xenobiotic response element a.k.a. dioxin response element) sequence in each of their promoter regions. The text in the paragraph beginning on page 251 of Ema et al. described a cell containing a recombinant DNA encoding that murine Ah receptor and a reporter plasmid encoding the enzyme chloramphenicol acetyl transferase (CAT) whose expression was under the control of an XRE. Figure 3 therein demonstrated the utility of such a cell in an assay for the detection of ligands to the Ah receptor. The cell of Ema et al differs from the cell and assay of the instant invention because Ema et al. utilized mammalian cells instead of yeast cell, Ema et al. utilized cells which presumably expressed Arnt endogenously and because Ema et al. used CAT as the reporter gene whereas the instant invention employs the lac Z gene product ß-galactosidase in this capacity.

The Mak et al. publication, in its entirety, described a yeast cell containing a recombinant DNA encoding the vertebrate nuclear progesterone receptor from chicken and a reporter plasmid encoding ß-galactosidase under the control of a receptor response element. Figures 6 and 7 on page 21616 of this publication disclosed the utility of such a cell in an assay for the detection of receptor ligand in a sample. The second full paragraph in the right column on page 21613 taught that "[b]aker's yeast (*Saccharomyces cerevisiae*) has been an attractive model for the study of

eukaryotic gene regulation due to its genetic simplicity and well defined transcription machinery". Because the Ah receptor of Ema et al. was functionally analogous to the progesterone receptor of Mak et al. in that each contains a ligand binding domain and a DNA binding domain in which, upon binding ligand, each receptor/ligand complex binds to a DNA response element, an artisan would have found it prima facie obvious to have substituted the Ah receptor and XRE of Ema et al. in place of the progesterone receptor and response element of Mak et al. to permit the detection of Ah receptor ligands in a sample by using the genetically simple yeast expression system. The Hoffman et al. publication has been further relied upon because it described a recombinant DNA encoding an Arnt protein. Because the Ema et al. publication shows that the presence of Arnt protein was known to be needed to obtain the transport of Ah receptor/ligand complex to the nucleus of a cell at the time of the instant invention, and artisan would have found it prima facie obvious to have included the recombinant DNA encoding the Arnt protein that was described by Hoffman et al. in a yeast cell in conjunction with a DNA encoding the Ah receptor and an XRE reporter plasmid as described by Ema et al. to permit the use of such a cell to detect Ah receptor ligand in a sample in a manner that was directly analogous to that which was described by Mak et al. prior to the time that the instant invention was made. Whether one employed CAT or ß-galactosidase as a reporter does not appear to distinguish the instant invention even though the Mak et al. publication shows that the use of ß-galactosidase as a reporter in yeast had been well established in the art at that time. Because the ligands for the Ah

receptor such as dioxin are found in the environment, an artisan would have found it prime facie obvious to have employed such cells to detect dioxin in air, soil or water.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (703) 308-4008. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Stephen Walsh, can be reached at (703) 308-2957.

Official papers filed by fax should be directed to (703) 308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. § 132 or which otherwise require a signature, may be used by Applicant and should be addressed to [**stephen.walsh@uspto.gov**].

All Internet e-mail communications will be made of record in the application file. PTO employees will not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. § 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on 25 February of 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JOHN ULM
PRIMARY EXAMINER
GROUP 1800